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09/475,704	12/30/1999	SUSAN W. BARNETT	1631.002	6738

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Chiron Corporation
Intellectual Property - R440
P.O. Box 8097
Emeryville, CA 94662-8097

EXAMINER	
WHITEMAN, BRIAN A	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 11/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/475,704	BARNETT ET AL.	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,4-10,24-43,49-60,63-66 and 68-75* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *69,71 and 73* is/are allowed.

6)☒ Claim(s) *2,4,5,7-10,24-43,49-60,63-66,68,70,72 and 74* is/are rejected.

7)☒ Claim(s) *6 and 75* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/20/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Non-Final Rejection

Claims 2, 4-10, 24-43, 49-60, 63-66, and 68-75 are pending.

Applicant's traversal filed on 8/25/05 is acknowledged and considered by the examiner.

Priority

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. However, as stated in the prior office action mailed on 9/14/01, the provisional application 60/114,495 upon which priority is claimed fails to provide adequate written support under 35 U.S.C. 112 for claims 2, 4-10, 24-43, 49-60, 63-66, and 68-75 of this application.

SEQ ID NO: 3 and 4 in Instant claims 2, 4-10, 24-43, 49-60, 63-66, 68-75 lack written support under 35 USC 112 first paragraph in provisional application '495.

Applicant's arguments filed 8/25/05 have been fully considered but they are not persuasive.

In response to applicant's argument that applicant disagree with the office's position that provisional 60/152,195 does not provide adequate written description for the pending claims inasmuch as the claimed subject matter is an obvious variant extension of what is described in co-owned 60/114,495, the argument is not found persuasive for the reason(s) set forth above. Nothing in the specification would lead one to the particular SEQ ID NOs as set forth in the instant application. "It is not sufficient for purposes of the written description requirement of Section 112 that the disclosure, when combined with the knowledge in the art, would lead one to speculate as to modifications that the inventor might have envisioned, but failed to disclose." *Lockwood v. American Airlines Inc.*, 41 USPQ2d 1961, 1966 (CAFC 1997).

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 6/20/05 was filed after the mailing date of the Non-Final Rejection on 5/31/05. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

It is acknowledged that in the previous office action, the examiner found applicant's argument persuasive and the 112 first paragraph written description and enablement was withdrawn. However, upon further consideration of the claims being amended in the response filed on 2/22/05 to recite a genus of HIV polypeptide (instead of HIV Gag polypeptide) that elicits a Gag-specific immune response, the claims are broader than what was previously claimed. Thus, 112 first paragraph rejection of the instant claims follows.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2, 4, 7-10, 24-43, 49-60, and 63-66 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 2, 4, 7-10, 24-43, 49-60, and 63-66, as best understood, are readable on a genus of a polynucleotide sequence encoding a HIV polypeptide that elicits a Gag-specific immune response, wherein the polynucleotide sequence encoding said HIV polypeptide comprises a nucleotide sequence having at least 90% sequence identity to the sequence presented in SEQ ID NO: 3 or 4, wherein the genus of polynucleotide sequences is not claimed in a specific biochemical or molecular structure that could be envisioned by one skilled in the art at the time the invention was made are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification contemplates production of a genus of a polynucleotide sequence encoding a polypeptide including an immunogenic HIV Gag polypeptide, wherein the polynucleotide sequence encoding said Gag polypeptide comprises a nucleotide sequence having

at least 90% sequence identity to the sequence presented in SEQ ID NO: 1, 2, 3, or 4. The term "an HIV polypeptide that elicits a Gag-specific immune response" indicates that claims 2 and 4 (and claims dependent therefrom that are not limited to SEQ ID NO: 3 and 4) are broader than claims directed to SEQ ID NO: 3 or 4. The specification does not define the term "an HIV polypeptide that elicits a Gag-specific immune response". The specification defines an "immunological response" as humoral and/or cellular immune response (page 14) and the cellular immune response could include a response with CD4+ cells and/or CD8+ cells. The specification and the prior art of record does not disclose which nucleotides or amino acids are considered essential for eliciting a Gag-specific immune response. For example, the specification does not disclose what peptides encoded by SEQ ID NOs: 3 or 4 elicit a Gag-specific immune response or what peptides from other HIV polypeptides elicit a Gag-specific immune response. Furthermore, the instant specification and the art of record teach that Gag proteins of HIV are necessary for the assembly of virus-like particles and HIV Gag proteins are involved in many stages of the life cycle of the virus including assembly, virion manufacture after particle release, and early post-entry step in virus replication. The role of HIV Gag proteins are numerous and complex (IDS, Freed, Virology, 1998). The specification contemplates that synthetic HIV Gag polypeptides can be measured for virus-like particle (VLP) production (page 29). The specification does not disclose how to make a genus of HIV polypeptides that elicit a Gag-specific immune response and is also at least 90% identical to the claimed sequences. One skilled in the art can envision a sequence that is at least 90% identical to the claimed SEQ ID NOs., but would be unable to determine if the sequence had a function that was considered part of the claimed genus of DNA molecules. For example, the claimed genus embraces HIV

polypeptides with distinct functions (e.g., Env, Pol, Rev, Protease, etc.) and the specification does not disclose how to make these polypeptides have Gag-specific immune activity.

In addition, on the amino acid level, there is even a larger variation than 90% identity to the polynucleotide sequences (70% with respect to substitutions and not including deletions and insertions), indicating a variation in the claimed genus of polynucleotide sequences. Determining 70% identity at the amino acid level from 90% at the polynucleotide level was based on the following: substituting 100 nucleotides of a 1,000 base pair polynucleotide sequence is a sequence with 90% identity to the 1,000 base pair polynucleotide sequence. The polypeptide sequence encoded by the polynucleotide sequence with 90% identity would have a polypeptide with 333 amino acids. Substitute one polynucleotide in 100 codons of the polynucleotide with 90% identity would be a polypeptide with 30% substitution. Thus, in view of the reasons set forth above and the numerous and complex functions of HIV polypeptides, the variation within the claimed genus of polynucleotide sequences, the specification does not disclose which activities of HIV correspond to the claimed genus of polynucleotides with 90% sequence identity to the claimed SEQ ID NOs 3 and 4.

It is apparent that on the basis of applicants' disclosure, an adequate written description of the invention defined by the claims requires more than a mere statement that it is part of the invention and reference to potential methods and/or molecular structures of molecules that are essential for the genus of polynucleotide sequences as claimed; what is required is the knowledge in the prior art and/or a description as to the availability of a representative number of species of biochemical or molecular structures of polynucleotide sequences that must exhibit the disclosed biological functions as contemplated by the claims.

The mere contemplation of the claimed genus in the specification is not sufficient to support the present claimed invention directed to a genus of a polynucleotide sequence encoding a HIV polypeptide that elicits a Gag-specific immune response, wherein the polynucleotide sequence encoding said polypeptide comprises a nucleotide sequence having at least 90% sequence identity to the sequence presented in SEQ ID NO: 1, 2, 3, or 4. The claimed invention as a whole is not adequately described if the claims require essential or critical elements, which are not adequately described in the specification and which is not conventional in the art as of applicant's effective filing date. Claiming a genus of polynucleotide sequences that must possess the biological properties as contemplated by applicants' disclosure without defining what means will do so is not in compliance with the written description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)). Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646 (1998). The skilled artisan cannot envision the detailed structure of a genus of a polynucleotide sequence encoding an HIV polypeptide that elicits a Gag-specific immune response, wherein the polynucleotide sequence encoding said polypeptide comprises a nucleotide sequence having at least 90% sequence identity to the sequence presented in SEQ ID NO: 3 or 4 that must exhibit the contemplated biological functions, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the structures and/or methods disclosed in

the as-filed specification. Thus, in view of the reasons set forth above, one skilled in the art at the time the invention was made would not have recognized that applicant was in possession of the claimed invention as presently claimed.

Applicant's arguments filed 2/22/05 have been fully considered but they are not persuasive.

Applicant asserts that "Gag-specific immune response" supplies the functional limitation for the claims; the assertion does not overcome the written description rejection because the instant claims read on a genus of HIV polypeptides that can elicit a Gag-specific immune response. The specification does not disclose a sufficient number of HIV polypeptides (HIV Pol, HIV nef, HIV, Rev, HIV, Gag, HIV protease) that would provide sufficient support for the claimed genus. Each HIV polypeptide embraced by the claimed genus indicates that there is substantial variation within the claimed genus. There is no structure-function correlation between a polynucleotide comprising SEQ ID NO: 3 and 4 and a genus of polynucleotides encoding a genus of HIV polypeptides that elicit a Gag-specific immune response.

In response to applicant's argument that the correlation between polypeptide structure and immunogenic function can tolerate many modifications. In other words essential residues are readily identifiable for enzymatic functions, any polypeptide can tolerate multiple substitutions at various residues while still retaining its immunogenic function (see Dr. Ulmer's Declaration of record, paragraph 18). The argument is not found persuasive because the specification and the prior art of record do not disclose multiple substitutions at various residues of HIV polypeptides other than HIV Gag that can elicit a Gag-specific immune response. In

addition, the specification does not disclose what amino acids of SEQ ID NO: 3 and 4 are necessary for a Gag-specific immune response.

In response to applicant's that in view of appendix A (PowerPoint slides presented by Christopher Low at the BioScience Forum on Thursday, September 9, 2004) and Example 14 of the PTO's "Synopsis of Application of Written Description Guidelines" written description requirement is satisfied because the instant specification discloses examples of sequences having claimed activity and methods of determining the presence or absence of such activity.

Applicant's argument with respect to Appendix A is not found persuasive because the claim language embraces a genus of polynucleotides that encode an HIV polypeptide that elicits a Gag-specific immune response. The specification does not provide sufficient description that a genus of HIV polypeptides can elicit a Gag-specific immune response.

Applicant's argument to Example 14 providing support for the claimed invention has already been addressed in a previous office action (pages 9-10). See office action mailed on 6/14/04. In addition, the example is directed to a nucleotide sequence with 95% identity encoding a protein with a specific activity, which is narrower than the claims reciting 90% identity. The specification does not define what is considered to be a Gag-specific immune response.

In response to applicant's argument that their description of particular sequence and recitation of these sequences in the claim distinguished the pending case from University of California v. Eli Lilly and every sequence can be envisioned exhibiting 90% identity from the reference sequences.

Applicant's argument is not found persuasive because while it is acknowledged the skilled artisan can envision a genus of polynucleotide sequences with 90% identity, the skilled artisan could not envision that a sufficient number of sequences exhibiting 90% identity to SEQ ID NO: 2 or 4 elicits a HIV-Gag specific immune response. The specification and the prior art of record do not disclose a genus of HIV polypeptides that elicit a Gag-specific immune response.

In response to applicant's argument that US Patent No. 6,602,705 has been issued with claims and disclosure highly analogous to those in the pending claim, the difference being that US Patent '705 claims polynucleotide sequences subtype C sequences and the guidance provided by this issued Patent regarding homology and assaying immunogenicity is virtually identical to that provided in the pending specification. Thus, '705 an issued and presumptively valid US Patent provides further evidence that the Patent Office considers claims such as those pending herein to be adequately described.

Applicant's argument is not found persuasive because every case is decided on its own merits. (*See In re Giolito*, 530 F.2d 397, 400, 188 USPQ 645, 648 (CCPA 1976):

"We reject appellants' argument that the instant claims are allowable because similar claims have been allowed in a patent. It is immaterial whether similar claims have been allowed to others." That other patents have been issued, based on different facts, is not evidence that the examiner's decision in this case, on these facts, is in error.

Claims 2, 4, 7-10, 24-43, 49-60, and 63-66 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making and using an expression cassette comprising the polynucleotide sequence set forth in SEQ ID NOs: 3 or 4, does not reasonably provide enablement for a polynucleotide sequence encoding an HIV polypeptide that

elicits a Gag-specific immune response, wherein the polynucleotide sequence encoding said polypeptide comprises a nucleotide sequence having at least 90% sequence identity to the sequence presented in SEQ ID NO: 3 or 4. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in In re Wands, 858 F.2d 731, 8USPQ2d 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The invention lies in the field of producing an immunogenic composition using an expression cassette comprising an HIV Gag polypeptide set forth in SEQ ID NOs: 3 or 4.

In the specification, the applicants contemplate: 1) Expression assays for the synthetic coding region of Gag and Gag-protease expression cassettes; 2) In vivo immunogenicity of Gag expression cassettes using plasmid DNA carrying the synthetic Gag expression cassette; 3) In vitro expression of recombinant alphavirus vectors or plasmid containing the synthetic Gag expression cassette; 4) In vivo immunogenicity of recombinant Sindbis replicon vectors containing Gag expression cassettes in mice by using intramuscular and subcutaneous routes.

The applicants further claim that these experiments will exhibit increased potency for induction of cytotoxic T-lymphocytes (CTL) response and humoral immune response by using the Gag expression cassette.

The specification provides sufficient guidance for one skilled in the art to make an immunogenic composition comprising an expression cassette comprising of SEQ ID NO: 3 or 4. However, the specification does not provide sufficient guidance and/or factual evidence for one skilled in the art to make and/or use a sequence

having at least 90% identity to any of the sequences presented as SEQ ID NO: 2 or 4 other than the sequences themselves.

The claimed invention is directed to a genus of polynucleotides encoding an HIV polypeptide that elicits a Gag-specific immune response, wherein the polynucleotide sequence comprises a nucleotide sequence having at least 90% sequence identity to the sequences presented in SEQ ID NO: 3 and 4. The specification does not define the term "an HIV polypeptide that elicits a Gag-specific immune response". The specification defines an "immunological response" as humoral and/or cellular immune response (page 14) and the cellular immune response could include a response with CD4+ cells and/or CD8+ cells. The specification does not disclose which nucleotides are considered essential for a Gag-specific immune response.

In addition, the nature of the invention is directed to a polynucleotide sequence encoding an HIV polypeptide that elicits a specific Gag immune response, wherein the polynucleotide comprises a nucleic acid sequence that has 90% identity to SEQ ID NO: 3 and 4. The scope of the invention is very broad, encompassing a large number of polynucleotide sequences that may or may not encode an HIV Gag polypeptide that may or may not have the desired activity. A search of SEQ ID NO: 4 (1509 nucleotides) indicates that SEQ ID NO: 3 (1479 nucleotides) is 84.6% identical to SEQ ID NO: 4. The same nucleotide search of SEQ ID NO: 4 indicates that it has 98.7% sequence identity to SEQ ID NO: 21 and 83.6% sequence identity to SEQ ID NO: 20. Other than the nucleic acid sequences of SEQ ID NO: 3 and 4 and

fragments of SEQ ID NO: 3 (SEQ ID NO: 1) or SEQ ID NO: 4 (SEQ ID NO: 2); and SEQ ID NO: 20 and 21, the specification fails to disclose any other nucleic acid sequences encoding a polypeptide with Gag activity. It is known for nucleic acids as well as proteins, for example, that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. The effects of these changes is largely unpredictable as to which ones have a significant effect versus not. Several publications document this unpredictability of the relationship between sequence and function, albeit that certain specific sequences may be found to be conserved over polypeptides of related function upon a significant amount of further research. See the following publications that support this unpredictability as well as noting certain conserved sequences in limited specific cases: Baker et al., Science, 294:pages 93-96, 2001); Attwood, T (*Science*, vol. 290, no. 5491, pp. 471-473, 2000); Gerhold et al., (*BioEssays*, vol. 18, no. 12, pp. 973-981, 1996); Russell et al., *Journal of Molecular Biology*, vol. 244, pp 332-350, 1994); and Wells et al., *Journal of Leukocyte Biology*, vol. 61, no. 5, pp. 545-550, 1997). Also, since the relationship of the sequence of a peptide and its tertiary structure (*e.g.* its activity) are not well understood and are not predictable (Ngo et al. The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495), it would require an undue amount of experimentation for one skilled in the art in view of the prior art to arrive at other sequences that have at least 90% sequence identity to the polypeptide encoded by SEQ ID NOs: 3 and 4 and still possess HIV Gag polypeptide activity.

In addition, the claims are broader than the guidance or factual evidence provided by the as-filed specification because the claims embrace a polypeptide with 70% identity to the HIV polypeptide encoded by SEQ ID NOs: 3 and 4. There is no guidance in the specification as to which amino acids encoded by the polynucleotide sequence set forth SEQ ID NO: 3 or SEQ ID NO: 4 may be changed while endogenous HIV Gag activity is retained and the HIV polypeptide is still immunogenic. As stated above, the teaching in the as-filed specification does not commensurate in scope with the claims because the breadth of the claims embrace a large number of possible sequences that differ from the polynucleotide sequence set forth in SEQ ID NO: 3 and 4. The claims are broader than the 90% limitation set forth in the claims because the polypeptide sequences embraced by the polynucleotide sequences having 90% identity to SEQ ID NO: 3 and 4 can have a substitution of at least 30% of the amino acids of the polypeptides encoded by the claimed sequences, which would be a substitution of up to 150 amino acids of the polypeptide encoded by either SEQ ID NO: 3 or 4. The number of single amino acid substitutions for an amino acid sequence encoded by the polynucleotide sequence set forth in SEQ ID NO: 3 or 4 is 9,500. The number of two amino acids substitutions for an amino acid sequence encoded by SEQ ID NO: 3 or 4 is over 9.0×10^7.

To determine the number of possible amino acid sequences encoded by the polypeptide encoded by the polynucleotide sequence set forth in SEQ ID NO: 3 or 4, N, with substitutions, one skilled in the art would use the formula $[(N=x^nL!/n!(L-n)!)$, where x=19 (number of possible amino acids that could

replace an amino acid at any one position in the polypeptide encoded by SEQ ID NO: 3 or 4), L=500 (estimated amino acid length of the polypeptide encoded by SEQ ID NO: 3 or 4), n=150,] or $1.1x10^{323}$ possible sequences.

This is a lower limit of the number of possible sequences because the claims also embrace insertions or deletions of amino acids in the polypeptide sequence encoded by SEQ ID NO: 3 or 4 that the equation does not take into account.

In conclusion, the instant specification and the claims coupled with the art of record at the time the invention was made only provide sufficient guidance and/or evidence to reasonably enable making and using an expression cassette comprising the polynucleotide sequence set forth in SEQ ID NOs: 3 and 4, does not reasonably provide enablement for a polynucleotide sequence encoding an HIV polypeptide that elicits a specific Gag immune response, wherein the polynucleotide sequence encoding said polypeptide comprises a nucleotide sequence having at least 90% sequence identity to the sequence presented in SEQ ID NO: 3 or 4. One would have to engage in a large quantity of excessive and undue experimentation in order to practice the claimed invention based on the In Re Wands Factors including the lack of guidance in the application's disclosure, the unpredictability of producing nucleotide sequences encoding a HIV polypeptide with 90% sequence identity to the claimed SEQ ID NOs. In addition, the prophetic examples as provided in the specification do not reasonably extrapolate to the full scope of the claimed invention because one skilled in the art would have to make a nucleotide sequence and determine if the sequence meets the limitations set forth in the claims.

Applicant's arguments filed 2/22/05 have been fully considered but they are not found persuasive because in view of the In Re Wands Factors, the instant specification does not provide sufficient guidance for one skilled in the art to practice the full scope of the claimed invention.

In response to applicant's argument that the presence of inoperative embodiments does not necessarily render a claimed nonenabled (See In re Angstadt, 537 F.2d 498, 504, 190 USPQ 214, 219, CCPA 1976, In re Cook, 439 F.2d 730, 735, 169 USPQ 298, CCPA 1971, Horton v. Stevens 7 USPQ 1245, 1247, Fed. Cir. 1988).

Applicant's argument is not found persuasive because while it is acknowledged that the claimed invention can embrace inoperable embodiments, it is the specification that should teach the skilled artisan what embodiments are inoperable/operable for practicing the full breadth of the claimed invention. See MPEP 2164.08. The specification does not teach the skilled artisan what embodiments are considered inoperable/operable for practicing the full scope of the claimed invention. For example, what HIV polypeptides selected from HIV Pol, HIV Rev, HIV protease, etc., embraced by the claimed genus are not considered operable. Thus, the skilled artisan would be further required to determine what polynucleotides exhibiting 90% identity to SEQ ID NO: 3 and 4 also have Gag-specific immune response. In view of the breadth of the genus and the absent of teaching in either the specification or the prior of record that assaying at least $1.1x10^{323}$ possible sequences for the desired was considered routine, the specification does not enabled the full scope of the claimed invention.

In response to applicant's argument that every single nucleotide species exhibiting 90% identity to SEQ ID NOs: 3 and 4 can be determined *a priori* and, as such, the entire genus of polynucleotide exhibiting 90% identity to these sequences is enabled by the specification as filed

(See Example N: DNA of the Patent Office's Training Material for Examining Patent Application with respect to First paragraph-enablement which states that even with a very large genus of sequences undue experimentation is not required to determine all members of the genus because each embodiment can be readily identified using the genetic code, synthesized using conventional methods, and used in the manner taught in the specification (page N-4).

The citation of Example N by the applicant is acknowledged and considered by the examiner, however, guidelines do not constitute substantive rulemaking and hence do not have the force and effect of law. The guidelines are designed to assist Office personnel in analyzing claimed subject matter. Any perceived failure by Office personnel to follow these guidelines is neither appealable nor petitionable. See MPEP 2163.

In view of example N, it would require undue experimentation to identify other HIV polypeptides that have Gag-specific immune response activity. It certainly would require undue experimentation to make their corresponding DNA. Therefore, it would be reasonable to conclude that it would require undue experimentation to make the entire scope of claimed inventions.

In response to applicant's argument that US Patent No. 6,602,705 has been issued with claims and disclosure highly analogous to those in the pending claim, the difference being that US Patent '705 claims polynucleotide sequences subtype C sequences and the guidance provided by this issued Patent regarding homology and assaying immunogenicity is virtually identical to that provided in the pending specification. Thus, '705 an issued and presumptively valid US Patent provides further evidence that the Patent Office considers claims such as those pending herein to be fully enabled.

Applicant's argument is not found persuasive because every case is decided on its own merits. (*See In re Giolito*, 530 F.2d 397, 400, 188 USPQ 645, 648 (CCPA 1976):

"We reject appellants' argument that the instant claims are allowable because similar claims have been allowed in a patent. It is immaterial whether similar claims have been allowed to others." That other patents have been issued, based on different facts, is not evidence that the examiner's decision in this case, on these facts, is in error.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (f) he did not himself invent the subject matter sought to be patented.

Claims 2, 4, 5, 24, 25, 41, 42, 68, and 74 remain rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter.

The claims from the instant application are directed to an expression cassette comprising a polynucleotide sequence operably linked to a promoter, wherein the polynucleotide sequence encodes an HIV Gag polypeptide with 90% sequence identity to the sequence encoding an HIV Gag polypeptide set forth in a particular SEQ ID NO: 3 and 4 and expression cassettes comprising control elements as set forth in instant claim 25.

Claim 72 from co-pending application 09/967,464 recites a microparticle comprises a vector comprising a heterologous nucleic acid sequence that encodes an HIV Gag polypeptide having a sequence having at least 90% identity to nucleotides 844-903 of SEQ ID NO: 63 (100% identity with SEQ ID NO: 3 of the instant invention), nucleotides 82-1512 of SEQ ID NO: 68 (and 99% identity to SEQ ID NO: 4 of the instant invention). Although the claim does not

specifically recite a promoter operably linked to the heterologous nucleic acid, the promoter would be required in the vector to express the heterologous nucleic acid because a promoter is required for the heterologous nucleic acid to be expressed in a cell. Claim 39 from '464 (which claim 72 depends from) recites an antigen selected from gag polypeptide.

Applicant's arguments filed 8/24/05 have been fully considered but they are not persuasive.

In response to applicant's argument that the claims from '464 are directed to different subject matter, the response is not found persuasive because the claims from '464 and the instant claims are both comprise a polynucleotide encoding a HIV polypeptide wherein the polynucleotide encodes an HIV polypeptide comprises a nucleotide sequence having at least 90% sequence identity to the sequence presented as Figure 1 or Figure 2 of the instant application. The language of the instant claims (expression cassette comprising) do not exclude the additional elements set forth in the claims from '464.

In response to applicant's argument that the '464 is not a proper reference against the pending case (See Court of Customs and Patent Appeals in In re Katz, 215 USPQ 14 (CCPA 1982), a reference can be used to establish a prima facie 102(f) rejection only if it was published before applicant's filing date. The pending application was filed in December 1999 while the cite reference was not published until 2003 (and, indeed, was not filed in 2001).

Applicant's argument is not found persuasive because there is nothing in In re Katz that recites that a reference has to be published before applicant's filing date. In addition, as stated in a previous office action, a rejection under 102(f) does not require an inquiry into the relative dates of a reference and the application. See MPEP 2137.

> It is incumbent upon the inventors named in the application, in reply to an inquiry regarding the appropriate inventorship under subsection (f), or to rebut a rejection under 35 U.S.C. 102(a) or (e), to provide a satisfactory showing by way of affidavit under 37 CFR 1.132 that the inventorship of the application is correct in that the reference discloses subject matter invented by the applicant rather than derived from the author or patentee notwithstanding the authorship of the article or the inventorship of the patent.

Claims 2, 4, 5, 24, 25, 41, 42, 68, and 74 remain rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter.

The claims from the instant application are directed to an expression cassette comprising a polynucleotide sequence operably linked to a promoter, wherein the polynucleotide sequence encodes an HIV Gag polypeptide with 90% sequence identity to the sequence encoding an HIV Gag polypeptide set forth in a particular SEQ ID NO: 3 and 4 and expression cassettes comprising control elements as set forth in instant claim 25.

The claims from US publication '453 (claims 26, 28, 31-34, 37-41, 45-50, and 72) claim a microparticle comprises a vector comprising a heterologous nucleic acid sequence that encodes an HIV Gag polypeptide. More specifically, claim 72 specifically recites a microparticle comprising a vector comprising a nucleic acid sequence having a sequence having at least 90% identity to nucleotides 844-903 of SEQ ID NO: 63 (100% identity with SEQ ID NO: 3 of the instant invention), nucleotides 82-1512 of SEQ ID NO: 68 (and 99% identity to SEQ ID NO: 4 of the instant invention). However, the claims from '453 do not specifically recite an expression construct comprising a promoter operably linked to the nucleic acid sequence as recited in instant

claims 24 and 25. However, a promoter is required to express the nucleic acid sequence in a cell. Claim 39 from '453 specifically recites the limitation in instant claim 42. Claim 37 recites the limitation in instant claim 43.

Applicant's arguments filed 8/24/05 have been fully considered but they are not persuasive for the reasons set forth above under the previous 102(f) rejection.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 2, 4, 5, 24, 25, 41-43, 68, and 74 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 26, 28, 31-50, and 72 of copending Application No. 09/967,464.

The claims from the instant application are directed to an expression cassette comprising a nucleotide sequence encoding a Gag polypeptide, wherein the nucleotide sequence encoding said Gag polypeptide comprises a nucleotide sequence having at least 90% sequence identity to claimed SEQ ID NOs: 3 and 4.

The claims from copending application '464 (claims 26, 28, 31-34, 37-41, 45-50, and 72) claim a microparticle comprises a vector comprising a heterologous nucleic acid sequence that encodes an HIV Gag polypeptide. More specifically, claim 72 specifically recites a microparticle comprising a vector comprising a nucleic acid sequence having a sequence having at least 90% identity to nucleotides 844-903 of SEQ ID NO: 63 (100% identity with SEQ ID NO: 3 of the instant invention), nucleotides 82-1512 of SEQ ID NO: 68 (and 99% identity to SEQ ID NO: 4 of the instant invention). However, the claims from '464 do not specifically recite an expression construct comprising a promoter operably linked to the nucleic acid sequence as recited in instant claims 24 and 25. However, one of ordinary skill in the art would understand that a promoter is required to express the nucleic acid sequence in a cell. Thus, it would have been obvious to one of ordinary skill in the art to operably linked a promoter to the nucleic acid sequence. Claim 39 from '464 specifically recites the limitation in instant claim 42. Claim 37 recites the limitation in instant claim 43. Thus, the instant claims and the claims from '464 are obvious variants of one another.

This is a provisional obviousness-type double patenting rejection.

Applicant's arguments filed 8/24/05 have been fully considered but they are not persuasive.

In response to applicant's argument that the claims from '464 are directed to different subject matter, the response is not found persuasive because the claims from '464 and the instant claims are both comprise a polynucleotide encoding a HIV polypeptide wherein the polynucleotide encodes an HIV polypeptide comprises a nucleotide sequence having at least 90% sequence identity to the sequence presented as Figure 1 or Figure 2 of the instant

application. The language of the instant claims (expression cassette comprising) do not exclude the additional elements set forth in the claims from '464.

Claims 2, 4, 5, 24, 25, 41-43, 68, and 74 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 26, 28, 31-50, and 72 of US pre-grant publication 2003/0138453.

The claims from the instant application are directed to an expression cassette comprising a nucleotide sequence encoding a Gag polypeptide, wherein the nucleotide sequence encoding said Gag polypeptide comprises a nucleotide sequence having at least 90% sequence identity to claimed SEQ ID NOs: 3 and 4.

The claims from US publication '453 (claims 26, 28, 31-34, 37-41, 45-50, and 72) claim a microparticle comprises a vector comprising a heterologous nucleic acid sequence that encodes an HIV Gag polypeptide. More specifically, claim 72 specifically recites a microparticle comprising a vector comprising a nucleic acid sequence having a sequence having at least 90% identity to nucleotides 844-903 of SEQ ID NO: 63 (100% identity with SEQ ID NO: 3 of the instant invention), nucleotides 82-1512 of SEQ ID NO: 68 (and 99% identity to SEQ ID NO: 4 of the instant invention). However, the claims from '453 do not specifically recite an expression construct comprising a promoter operably linked to the nucleic acid sequence as recited in instant claims 24 and 25. However, one of ordinary skill in the art would understand that a promoter is required to express the nucleic acid sequence in a cell. Thus, it would have been obvious to one of ordinary skill in the art to operably linked a promoter to the nucleic acid sequence. Claim 39 from '453 specifically recites the limitation in instant claim 42. Claim 37 recites the limitation in

instant claim 43. Thus, the instant claims and the claims from '453 are obvious variants of one another.

This is a provisional obviousness-type double patenting rejection.

Applicant's arguments filed 8/24/05 have been fully considered but they are not persuasive because the argument was already addressed in the examiner's response to the previous provisional double patenting rejection.

Claims 2 and 24-25 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over either claims 26, 28, 31-50, and 72 of copending Application No. 09/967,464 or claims 26, 28, 31-50, and 72 of US pre-grant publication 2003/0138453 in view of Tartaglia et al. (US 5,990,091) and Corbin et al. (US 6,489,542).

The claims from either '464 or '453 do not specifically recite an expression cassette comprising control elements as recited in instant claims 24 and 25.

However, Tartaglia et al. teach making and using a plasmid comprising a polynucleotide encoding HIV polypeptide. Tartaglia does not specifically teach the control elements in instant claim 25. However, Corbin teaches that the control elements recited in instant claim 25 were readily available to one of ordinary skill in the art for making a plasmid comprising the control elements. Thus, it would have been obvious to one of ordinary skill in the art to make and use a plasmid comprising the control elements recited in instant claim 25 for expressing the polynucleotide in a cell. Thus, the instant claims 2, 24 and 25 are obvious variants of the claims from either '464 or '453 in view of Tartaglia et al. and Corbin et al.

This is a provisional obviousness-type double patenting rejection.

Applicant's arguments filed 8/24/05 have been fully considered but they are not persuasive because the argument was already addressed in the examiner's response to the previous provisional double patenting rejection.

Claims 2 and 24-26 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over either claims 26, 28, 31-50, and 72 of copending Application No. 09/967,464 or claims 26, 28, 31-50, and 72 of US pre-grant publication 2003/0138453 in view of Tartaglia et al. (US 5,990,091) and Corbin et al. (US 6,489,542) either Sikic et al. (US 5,830,697) or Dubensky et al. (US 6,391,632).

The claims from either '464 or '453 and Tartaglia and Corbin do not specifically recite an expression cassette comprising control elements as recited in instant claim 26.

However, the promoters recited in instant claim 26 were readily available to one of ordinary skill in the art for making a plasmid comprising the promoters as exemplified by Sikic et al., column 4 and Dubensky et al., columns 22, 26, and 87-88. Thus, it would have been obvious to one of ordinary skill in the art to make and use a plasmid comprising the promoters recited in instant claim 26 for expressing the polynucleotide in a cell. Thus, the instant claims 2 and 24-26 are obvious variants of the claims from either '464 or '453 in view of Tartaglia et al. and Corbin et al. and either Sikic et al. or Dubensky et al.

This is a provisional obviousness-type double patenting rejection.

Applicant's arguments filed 8/24/05 have been fully considered but they are not persuasive because the argument was already addressed in the examiner's response to the previous provisional double patenting rejection.

Claims 2 and 27-40 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over either claims 26, 28, 31-50, and 72 of copending Application No. 09/967,464 or claims 26, 28, 31-50, and 72 of US pre-grant publication 2003/0138453 in view of ATCC catalog of cell lines and hybridomas (7th edition, Maryland, 1992, pages 70, 79, 148, 150, 158, 164, 194, 299, 308, and 456); Helting et al. (US 5,470,720); and Adams et al. (IJ-1).

The claims from either '464 or '453 do not specifically recite a cell comprising the expression cassette as recited in instant claims 27-40.

However, the cell lines recited in instant claims 27-40 were readily available to one of ordinary skill in the art as taught in the instant specification (pages 30-31) and the prior art as exemplified by ATCC catalog of cell lines and hybridomas, Helting et al. and Adams et al. for producing a cell line selected from instant claims 27-40. Thus, it would have been obvious to one of ordinary skill in the art to make and use a cell comprising a plasmid comprising the promoters recited in instant claims 27-40 for expressing the polynucleotide in a cell in vitro. Thus, the instant claims 2 and 27-40 are obvious variants of the claims from either '464 or '453 in view of ATCC catalog of cell lines and hybridomas, Helting et al. and Adams et al.

This is a provisional obviousness-type double patenting rejection.

Applicant's arguments filed 8/24/05 have been fully considered but they are not persuasive because the argument was already addressed in the examiner's response to the previous provisional double patenting rejection.

Claims 68 and 70 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over either claims 26, 28, 31-50, and 72 of copending Application No. 09/967,464 or claims 26, 28, 31-50, and 72 of US pre-grant publication 2003/0138453 in view of Rovinski et al (BS-1).

The claims from either '464 or '453 do not specifically recite the expression cassette further comprising a nucleotide sequence encoding an HIV protease polypeptide.

However, Rovinski teaches recombinant nucleic acid encoding HIV gag and HIV protease and using the nucleic acid to produce a non-infectious retrovirus. Thus, it would have been obvious to one of ordinary skill in the art to make and use a vector comprising a nucleic acid encoding an HIV gag (SEQ ID NO: 3) and a nucleic acid encoding an HIV protease to produce a retrovirus as taught by Rovinski. Thus, the instant claims 68 and 70 are obvious variants of the claims from either '464 or '453 in view of Rovinski.

This is a provisional obviousness-type double patenting rejection.

Applicant's arguments filed 8/24/05 have been fully considered but they are not persuasive because the argument was already addressed in the examiner's response to the previous provisional double patenting rejection.

Claims 68 and 72 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over either claims 26, 28, 31-50, and 72 of copending Application No. 09/967,464 or claims 26, 28, 31-50, and 72 of US pre-grant publication 2003/0138453 in view of Rovinski et al. (BE-1).

The claims from either '464 or '453 do not specifically recite the expression cassette further comprising a nucleotide sequence encoding an HIV polymerase polypeptide.

However, Rovinski teaches recombinant nucleic acid encoding HIV gag and HIV polymerase. Rovinski teaches producing a non-infectious HIV particle comprising Env gene product, Gag gene product, Pol gene product and one antigenic marker (column 2). Thus, it would have been obvious to one of ordinary skill in the art to make and use a vector comprising a nucleic acid encoding an HIV gag (SEQ ID NO: 3) and a nucleic acid encoding an HIV polymerase to produce HIV particles. Thus, the instant claims 68 and 72 are obvious variants of the claims from either '464 or '453 in view of Rovinski.

This is a provisional obviousness-type double patenting rejection.

Applicant's arguments filed 8/24/05 have been fully considered but they are not persuasive because the argument was already addressed in the examiner's response to the previous provisional double patenting rejection.

Claims 2, 4, 5, 24-26, 41-43, 68, and 74 remain directed to an invention not patentably distinct from claims of commonly assigned copending application 09/967,464 and pre-grant US publication 2003/0138453. Specifically, for the reasons set forth under the provisional double patenting rejection.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned us application, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 35 U.S.C. 103(c) and 37 CFR 1.78(c) to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

Applicant's arguments filed 8/24/05 have been fully considered but they are not persuasive because the argument was already addressed in the examiner's response to the provisional double patenting rejection.

Response to Arguments

Applicant's arguments, see page 2, filed 8/25/05, with respect to 102(e) rejection have been fully considered and are persuasive. The rejection of claims 2, 4, 7, 24, 25, 27, 28, and 41-43 has been withdrawn.

Applicant's arguments, see pages 4-5, filed 8/25/05, with respect to 103(a) rejections have been fully considered and are persuasive. The rejections of claims 2, 4, 5, 7-10, 24-43, 49-60, 63-66, 68, 70, 72, and 74 has been withdrawn.

Conclusion

Claims 6, 69, 71, 73, and 75 are free of the prior art of record.

Claims 6 and 75 remain objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (571) 272-0764. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, acting SPE – Art Unit 1635, can be reached at (571) 272-0811.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Brian Whiteman
Patent Examiner, Group 1635